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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/524,738	GOLETZ ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 January 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *53-60,63-74 and 81-99*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/MISOOK YU/
Primary Examiner, Art Unit 1642

Continuation of 11. does NOT place the application in condition for allowance because: Claims 53, 55, 57, 63, 65, 67, 69, 71, 73, 81-85, 87, 89, 91, 92, 95, 96, and 99 remain rejected under 35 U.S.C. 102(b) as being anticipated by Mivechi (Cancer Research, April 1989, 49: 1954-1958), as evidenced by Lozzio and Lozzio (Blood , March 1975, 45(3): 321-334), for the reasons stated in the Office Action of 2/6/08, the reasons stated in the Office Action of 8/4/08, and for the reasons set-forth below.

The claims are product-by-process claims drawn to lysate "obtainable" by processes involving inducing necrosis of NM-F9 or NM-D4 tumor cells. It is noted that the specification discloses: "The term "NM-F9" (also referred herein as "F9" or "TF-positive F9 cells") or "NM-D4" means cell lines or cells derived from the human myelogenous leukemia cell line K562 (ATCC: CCL-243)" (see last three lines on page 22).

Mivechi teaches vaccine compositions comprising lysates from cells derived from human myelogenous leukemia cell line K562 that have gone through necrosis after being treated at 45C/10 min, 42C/2 hr, or 41C/2 hr see page 1954, in particular). In view of page 22 of the instant specification, the cells taught by Mivechi are NM-F9 and NM-D4 cells. Further, as evidenced by Lozzio and Lozzio, the cells taught by Miyechi are genetically engineered, mutated, or infected by oncogenic viruses (see page 326 of Lozzio and Lozzio, in particular). The claimed lysate is not limited to lysate that has been "obtained" by lysing NM-F9 or NM-D4 tumor cell lines with the recited accession numbers and is not limited to lysate that induces a humoral immune response to TF antigen. Rather, the claimed lysate is limited to lysate that is "obtainable" by methods using NM-F9 or NM-D4 tumor cell lines with said accession numbers. K562 cells are parental cells of NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims. As parental cells of said tumor cell lines, the K562 cells and the NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims are comprised of nearly identical matter. Because Mivechi teaches vaccine compositions comprising lysates from K562 cells that have gone through necrosis after being treated at 45C/10 min, 42C/2 hr, or 41C/2 hr (see page 1954, in particular) and because said cells are (1) parental cells of and (2) are comprised of nearly identical matter as the NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims, the lysate of Mivechi would comprise lysate that is "obtainable" by inducing necrosis of NM-F9 or NM-D4 tumor cell lines with treatment at 45C/10 min, 42C/2 hr, or 41C/2 hr and lysing said cells so as to obtain a lysate that is capabled of inducing a humoral immune response against TF antigen.

Although the combined teachings do not specify the percentage of the tumor cells that are necrotic after induction of necrosis, the percentage of cells expressing membrane-bound HSP 70 protein, or cells treated at 45.5 degrees C, the claimed products appear to be the same as the prior art, absent a showing of unobvious differences.

In the Reply of 1/2/09, Applicant states that the claims have been amended to recite lysates that are capable of inducing a humoral response to TF antigen. Applican further argues that Mivechi neither teaches a vaccine nor lysates capable of inducing a humor immune response to TF antigen. Applicant further argues that one of skill in the art would not equate the lysates of Mivechi, produced from heat-treated K562 cells and to be used for SDS-PAGE, with lysates suitable for vaccination and/or for loading into dendritic cells. Applicant further argues that Mivechi does not teach vaccine compositions or cancer immunotherapy.

The amendments to the claims and the arguments found in the Reply of 1/2/09 have been carefully considered, but are not deemed persuasive. In regards to the argument that Mivechi does not teach a vaccine (see instant claim 57), use of the lysate as a vaccine is an intended use and not a limitation to claims.

In regards to the argument that Mivechi does not teach lystates capble of inducing a humoral response to TF antigen, lysate encompassed by the instant claims is not requied to be capable of inducing a humoral response to TF antigen. Rather, the claimed lysate is limited to lysate that is "obtainable" by lysing cells so as to obtain a lysate that is capable of inducing a humoral immune response against TF antigen. The lysate taught by Mivechi would comprise lysate "obtainable" by lysing cells so as to obtain a lysate that is capable of inducing a humoral immune response against TF antigen.

In regard to arguments that one of skill in the art would not equate the lysates of Mivechi with lysates suitable for vaccination and/or for loading into dendritic cells and that Mivechi does not teach vaccine compositions or cancer immunotherapy, intended uses of vaccination, loading into dendritic cells, and cancer immunotherapy are not considered limitations to the claimed products.

Claims 53-60, 67-74, 81-83, 86, and 91-99 remain rejected under 35 U.S.C. 103(a), as being unpatentable over Subjeck et al (US Patent 6,984,384 B1; filed 9/29/00) in view of Yoshima et al (JBC, September 1998, 273(39): 25466-25471), for the reasons stated in the Office Action of 2/6/08, the reasons stated in the Office Action of 8/4/08, and for the reasons set-forth below.

Subjeck et al teaches a lysate of mutated tumor cells derived from a patient and a composition of said lysate obtainable by a process comprising the steps of: (a) inducing necrosis of tumor cells by subjecting the cells to a temperature of 43C for two hours; and (b) lysing said necrotic tumor cells (see column 19, in particular). It is noted that the instant claims describing lysate as a "pharmaceutical composition" or a "vaccine composition" are merely describing an intended use of the claimed lysate compositions. It is noted that statements of intended purposes or uses are not considered limitations because they merely state an intended use of the invention rather than any distinct definition of any of the claimed invention's limitations (see Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). Recitation of statements describing the claimed product as a medicament intended to treat a condition are not given patentable weight and are not limitations to the claims. Subjeck et al further teaches compositions comprising immature and mature dendritic cells loaded with the lysate of mutated tumor cells derived from a patient obtainable by a process comprising the steps of: (a) inducing necrosis of tumor cells by subjecting the cells to a temperature of 43C for two hours; and (b) lysing said necrotic tumor cells (columns 26-27, in particular). Subjeck et al further teaches comprising immature and mature dendritic cells

loaded with the lysate of mutated tumor cells combined with an adjuvant (column 23, in particular).

Subjeck et al does not specifically teach a product wherein NM-F9 or NM-D4 tumor cells are used to make the product, the percentage of cells necrotic after induction of necrosis, or the percentage of cells expressing membrane-bound HSP 70 protein. However, these deficiencies are made up in the teachings of Yoshima et al.

Yoshima et al teaches cells that are genetically engineered, mutated or infected by oncogenic viruses and derived from the human myelogenous leukemia cell line K562 (see left column of page 25467, in particular). Yoshima et al further teaches that HSP 70 expression is undetectable in untreated K562 tumor cells (see Figure 1, in particular). Yoshima et al further teaches that HSF1, in response to heat shock, activates expression of HSP70 in K562 tumor cells (see right column of page 25466, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to use the K5624 tumor cells taught by Yoshimda et al as the mutated tumor cells when producing the vaccine taught by Subjeck et al because Subjeck et al teaches that HSP70 induced by heat shocking tumor cells would function in a lysed cell vaccine by stabilizing peptides (see column 11, in particular) and Yoshimda et al teaches HSP70 is induced in K562 tumor cells upon heat-shock (see right column of page 25466, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using the cells taught by Yoshimda et al as the mutated tumor cells in the vaccine taught by Subjeck et al because Subjeck et al teaches how to use cells to produce said vaccine (see column 19, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Although the combined teachings do not specify the percentage of the tumor cells that are necrotic after induction of necrosis or the percentage of cells expressing membrane-bound HSP 70 protein, the claimed product appear to be the same as the prior art, absent a showing of unobvious differences. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the products produced by the method of the prior art do not possess the same material and structural characteristics of the claimed products. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed products are different from that taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989).

In the Reply of 1/2/09, Applicant states that the amended claims state that the lysates are capable of inducing a humoral immune response against TF antigen and one of skill in the art would not predict Yoshima's K562 cells elicit a response against the TF antigen.

The amendments to the claims and the arguments found in the Reply of 1/2/09 have been carefully considered, but are not deemed persuasive. In regards to the argument that Yoshima's K562 cells would not predictably elicit a response against the TF antigen, lysate encompassed by the instant claims is not required to be capable of inducing a humoral response to TF antigen. Rather, the claimed lysate is limited to lysate that is "obtainable" by lysing cells so as to obtain a lysate that is capable of inducing a humoral immune response against TF antigen. The lysate of Yoshima's K562 cells would comprise lysate "obtainable" by lysing cells so as to obtain a lysate that is capable of inducing a humoral immune response against TF antigen.

Claims 53-60, 63-74, and 81-99 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mivechi (Cancer Research, April 1989, 49: 1954-1958), as applied to claims 53, 55, 57, 63, 65, 67, 69, 71, 73, 81-85, 87, 89, 91, 92, 95, 96, and 99 above, and further in view of Subjeck et al (US Patent 6,984,384 B1; filed 9/29/00), for the reasons stated in the Office Action of 2/6/08, the reasons stated in the Office Action of 8/4/08, and for the reasons set-forth below.

The teachings of Mivechi are described above.

Mivechi does not specifically teach dendritic cells loaded with lysates. However, this deficiency is made up in the teachings of Subjeck et al.

Subjeck et al teaches a lysate of mutated tumor cells derived from a patient and a composition of said lysate obtainable by a process comprising the steps of: (a) inducing necrosis of tumor cells by subjecting the cells to a temperature of 43C for two hours; and (b) lysing said necrotic tumor cells (see column 19, in particular). It is noted that the instant claims describing lysate as a "pharmaceutical composition" or a "vaccine composition" are merely describing an intended use of the claimed lysate compositions. It is noted that statements of intended purposes or uses are not considered limitations because they merely state an intended use of the invention rather than any distinct definition of any of the claimed invention's limitations (see Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). Recitation of statements describing the claimed product as a medicament intended to treat a condition are not given patentable weight and are not limitations to the claims. Subjeck et al further teaches compositions comprising immature and mature dendritic cells loaded with the lysate of mutated tumor cells derived from a patient obtainable by a process comprising the steps of: (a) inducing necrosis of tumor cells by subjecting the cells to a temperature of 43C for two hours; and (b) lysing said necrotic tumor cells (columns 26-27, in particular). Subjeck et al further teaches compositions comprising immature and mature dendritic cells loaded with the lysate of mutated tumor cells combined with an adjuvant (column 23, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to use the tumor cells taught by Mivechi as the mutated tumor cells when producing the vaccine taught by Subjeck et al because Subjeck et al teaches that HSP70 induced by

heat shocking tumor cells would function in a lysed cell vaccine by stabilizing peptides (see column 11, in particular) and Mivechi teaches HSP70 is induced in the tumor cells of Mivechi upon heat-shock (see left column of page 1955, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using the cells taught by Mivechi as the mutated tumor cells in the vaccine taught by Subjeck et al because Subjeck et al teaches how to use cells to produce said vaccine (see column 19, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results .

In the Reply of 1/2/09, Applicant argues that the instant claims are not obvious over the cited art because neither Mivechi nor Subjeck contains a teaching, suggestion, or motivation to generate lysates capable of eliciting a humoral immune response against the TF antigen.

In regards to the argument that the instant claims are not obvious over the cited art because neither Mivechi nor Subjeck contains a teaching, suggestion, or motivation to generate lystates capable of eliciting a humoral immune response against TF antigen, lysate encompassed by the instant claims is not required to be capable of inducing a humoral response to TF antigen. Rather, the claimed lysate is limited to lysate that is "obtainable" by lysing cells so as to obtain a lysate that is capable of inducing a humoral immune response against TF antigen. The lysate taught by the combined teachings of Mivechi and Subjeck would comprise lysate "obtainable" by lysing cells so as to obtain a lysate that is capable of inducing a humoral immune response against TF antigen.